Tuning and Predicting Mesh Size and Protein Release from Step Growth Hydrogels.

Journal: Biomacromolecules

Publication Year: 2017

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PubMed link: 28850788

Funding Grants: Tunable hydrogels for therapeutic delivery of multipotent stem cells.

Public Summary:
Hydrogel-based depots are of growing interest for release of biopharmaceuticals (for example growth factors); however, selection of hydrogel compositions that will retain proteins of interest and provide desired release profiles remains elusive. In this manuscript we have established a new tool for the facile assessment of protein release from hydrogels and applied it to evaluate the effectiveness of mesh size estimations on predicting protein retention or release. With this knowledge, hydrogels were designed for the controlled release of a therapeutically relevant growth factor, PDGF-BB.

Scientific Abstract:
Hydrogel-based depots are of growing interest for release of biopharmaceuticals; however, a priori selection of hydrogel compositions that will retain proteins of interest and provide desired release profiles remains elusive. Toward addressing this, in this work, we have established a new tool for the facile assessment of protein release from hydrogels and applied it to evaluate the effectiveness of mesh size estimations on predicting protein retention or release. Poly(ethylene glycol) (PEG)-based hydrogel depots were formed by photoinitiated step growth polymerization of four-arm PEG functionalized with norbornene (PEG-norbornene, 4% w/w to 20% w/w, Mn approximately 5 to 20 kDa) and different dithiol cross-linkers (PEG Mn approximately 1.5 kDa or enzymatically degradable peptide), creating well-defined, robust materials with a range of mesh sizes estimated with Flory-Rehner or rubber elasticity theory (approximately 5 to 15 nm). A cocktail of different model proteins was released from compositions of interest, and sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) was used to facilely and quantitatively analyze temporal release profiles. Mesh size was predictive of retention of relatively large proteins and release of relatively small proteins. Proteins with diameters comparable to the mesh size, which is often the case for growth factors, were released by hindered diffusion and required experimental assessment of retention and release. With this knowledge, hydrogels were designed for the controlled release of a therapeutically relevant growth factor, PDGF-BB.